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Moderate-to-Severe Pain after Knee Arthroplasty: A Retrospective Study of Incidence and Risk Factors

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Background: Knee arthroplasty is one of the most painful orthopedic surgeries. In daily clinical practice, different analgesic techniques are used for postoperative pain control.

Objective: To investigate the incidence and risk factors for moderate-to-severe pain in patients undergoing knee arthroplasty.

Materials and Methods: The medical records of 400 patients who underwent knee arthroplasty were retrospectively reviewed. The intensity of postoperative pain was assessed by numeric rating scale (NRS) at every 12-hour interval for 72 hours after surgery. Based on maximum NRS score during the first postoperative day, patients were divided into group moderate-to-severe pain (NRS score≥4) and group no or mild pain (NRS score<4). Risk factors associated with moderate-to-severe pain were analyzed.

Results: Approximately half of patients experienced moderate-to-severe pain on the first postoperative day. The independent risk factors for moderate-to-severe pain were preoperative pain (adjusted odds ratio [AOR] 2.10, 95% confidence interval [CI] 1.31-3.35, *p*=0.002) and type of anesthesia (AOR, 2.79 for spinal anesthesia plus periarticular infiltration and peripheral nerve block group; 95% CI, 1.39-5.60; *p*=0.004, and AOR, 3.42 for general anesthesia plus periarticular infiltration with or without peripheral nerve block group; 95% CI, 1.27-9.20; *p*=0.015; when using group spinal anesthesia plus intrathecal morphine, periarticular infiltration and peripheral nerve block as a reference).

Conclusions: An approximately 50% of patients had moderate-to-severe pain on the first postoperative day. Preoperative pain and type of anesthesia were identified as independent risk factors for moderate-to-severe pain.

Keywords: Knee arthroplasty, Moderate-to-severe pain, Incidence, Risk factors

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Introduction

Knee arthroplasty (KA) is one of the most commonly performed joint replacement surgeries. It is considered for patients who have degeneration of the knee joint, such as osteoarthritis, rheumatoid arthritis, and arthritis from severe knee injury.[1-3] Total knee arthroplasty (TKA) replaces the whole knee joint with a prosthesis, whereas unicompartmental knee arthroplasty (UKA) replaces only the most affected parts of the knee joint.[4] Although UKA is less invasive compared to TKA, a high level of pain after UKA has been described.[5] Both TKA and UKA are frequently reported to be the most painful orthopedic surgeries because of involving bone resection and cutting of surrounding tissues. These painful stimuli can activate pain sensitive areas of the knee joint, including the retinaculum, anterior synovium, fat pad, joint

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capsule, and soft tissues around the knee joint.[6-8] Uncontrolled severe postoperative pain may result in delayed rehabilitation, development of chronic persistent postsurgical pain, decreased quality of life, and reduced patient satisfaction.[9-11]

Postoperative pain is a major concern after surgery. Previous study found that more than half of patients suffered moderate to severe pain after TKA, and that approximately half of patients had night pain.[12] Pain management after KA is challenging. There are wide variations in the choice of anesthetic and analgesic techniques performed, such as general anesthesia, neuraxial anesthesia with or without intrathecal opioids, single-dose or continuous peripheral nerve block, periarticular infiltration or local infiltration analgesia, and combinations of these techniques. It is unclear whether these methods provide adequate pain control after this type of surgery. Previously published studies mainly compared different anesthetic and analgesic techniques, and they mostly comprised traditional randomized controlled trials (RCTs) that included narrowly selected populations that were studied under a controlled clinical environment.[13] The results of these studies sometimes have limited generalizability to everyday clinical practice. Alternatively, study in routine clinical practice may provide additional data for optimal pain management that is clinically significant.

Thus, this retrospective study aimed to investigate the incidence of moderate to severe pain among patients who underwent KA performed in routine clinical practice. The secondary objective was to identify risk factors for moderate to severe pain during the first 24 hours postoperatively.

Materials and Methods

Patients

After receiving institutional review board approval (COA no. Si 658/2017), a retrospective chart review study was conducted during the January 2017 to October 2017 study period. The electronic medical records with International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure code for knee replacement (8154) were identified. All consecutive patients who underwent UKA or TKA were eligible for inclusion. Patients who underwent simultaneous bilateral KA or revision KA, who underwent KA due to bone tumor, who were admitted to the intensive care unit (ICU) after surgery, or who had incomplete electronic medical records were excluded.

In daily clinical practice, there is substantial variability in the anesthetic and analgesic techniques used for KA at our center. For statistical analysis, in order to reduce bias associated with the small number of patients in some groups, all patients were divided into three main groups according to type of anesthesia. As seen in Table 1, patients receiving spinal anesthesia (SA) plus intrathecal morphine (MO), periarticular infiltration (PI) and peripheral nerve block (NB) were grouped together as SAMO-PI-NB group (n=71). Patients receiving SA plus PI and NB were grouped together as SA-PI-NB group (n=299). Patients receiving general anesthesia (GA) plus PI with or without NB were grouped together as GA-PI/NB group (n=30). Regarding NB, adductor canal block (ACB) or femoral nerve block (FNB) was used in combined analgesia for KA.

Data collection

The following data were collected from the electronic medical records by two reviewers: patient demographics, such as age, gender, weight, and height; American Society of Anesthesiologists classification; type, duration, and date of surgery; tourniquet time; type of anesthesia; preoperative and postoperative pain evaluation by numerical rating scale (NRS); postoperative analgesia regimens and opioid requirements for breakthrough pain; opioid-related adverse effects, such as respiratory depression, nausea, vomiting, pruritus, and dizziness; and, length of hospital stay. All retrieved data were cross-checked before being entered into the database for statistical analysis.

Outcome measures

Pain severity was measured using a NRS ranging from 0 (no pain) to 10 (worst imaginable pain).

The maximum NRS scores during the following postoperative time intervals were recorded: during the first 12 hours after surgery, during 12-24 hours after surgery, during 24-36 hours after surgery, during 36-48 hours after surgery, during 48-60 hours after surgery, and during 60-72 hours after surgery. Pain scores were classified, as follows: no pain (NRS score=0), mild pain (NRS score=1-3), moderate pain (NRS score=4-6), and severe pain (NRS score=7-10). Moderate-to-severe pain (NRS score≥4) was defined as inadequate pain control because a cut-off value of 4 or more was previously identified as pain requiring supplemental analgesics.[14, 15] Incidences of moderate-to-severe pain in each postoperative time intervals were calculated.

Postoperative analgesic drugs prescribed during 72 hours after surgery were recorded. However, in our center, there are analgesic treatment disparities for acute postoperative pain, such as opioids, paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, and a combination of these drugs. For further analysis, in order to reduce bias associated with the small number of patients in some groups, patients were divided into two groups according to postoperative analgesics used (Table 1). Patients who received a combination of four classes of analgesic drugs, including opioids, acetaminophen, NSAIDs, and gabapentinoids were grouped together as group analgesics 4 drugs (n=275). The remaining patients who received a combination of analgesic drugs < 4 drugs were grouped together as group analgesics < 4 drugs (n=125).

For risk factor analysis, all patients were divided into two main groups according to the maximum NRS score reported during the first postoperative day (Table 1). Patients with a maximum NRS score of ≥ 4 during the first 12 hours, and during 12-24 hours after surgery were allocated to the moderate-to-severe pain group (n=123). The remaining patients were allocated to the no or mild pain group (n=277). Then, factors associated with moderate-to-severe pain were analyzed.

Sample size calculation and statistical analysis

Previous studies[12, 16-18] reported the average incidence rate of moderate-to-severe pain to be 37.5% on the first postoperative day among patients who underwent KA. Using these data, the sample size was calculated using a two-sided 95% confidence interval for a single proportion that extends 0.050 to both sides of the estimated proportion of 0.375. A minimum sample size of 361 patients was calculated. To compensate for an estimated dropout rate for any reason of 10%, the minimum sample size was increased to 398 patients.

All statistical analyses were performed using PASW Statistics version 18.0 (SPSS, Inc., Chicago, IL, USA). Continuous data are presented as mean±standard deviation for normally distributed data, and as median and range (minimum and maximum) for non-normally distributed data. Categorical data are presented as frequency and percentage. All variables in patients with postoperative moderate-to-severe pain versus those with no or mild pain were analyzed by univariable analysis using chi-square test, Fisher's exact test, or independent *t*-test, as appropriate. Those variables with *p*-values less than 0.2 in univariable analysis were included in multivariable analysis using multiple logistic regression. Odds ratio (OR) and adjusted odds ratio (AOR) with their respective 95% confidence intervals (CI) were reported. Cumulative morphine consumption was analyzed by Kruskal-Wallis with Dunn's pairwise tests. Statistical significance was set at a *p*-value less than 0.05.

Results

The electronic medical records of 478 consecutive patients who underwent KA during the study period were retrospectively reviewed for eligibility. Of those, 78 patients were excluded due to receiving patient-controlled analgesia after surgery (n=42), undergoing bilateral KA (n=28), having a diagnosis of knee bone tumor (n=3), having ICU admission after surgery (n=3), and having incomplete data (n=2). Of the remaining 400 patients, 319 (79.8%) underwent TKA, and 81 (20.2%) underwent UKA. The demographic and clinical data of the included patients are shown in Table 1. The median length of hospital stay was 5 days (2-29 days).

Table 1 Demographics and clinical data

	Total (n = 400)	Maximum NRS < 4 (n = 277)	Maximum NRS ≥ 4 (n = 123)	*p*-value
Age (years)	68.0 ± 8.3	68.3 ± 8.5	67.4 ± 8.0	0.345
Gender, female	344 (86.0)	239 (86.3)	105 (85.4)	0.808
Body mass index (kg/m^2)	27.5 ± 4.7	27.4 ± 4.7	27.7 ± 4.6	0.558
ASA physical status				0.392
1	17 (4.3)	12 (4.3)	5 (4.1)	
2	262 (65.5)	187 (67.5)	75 (61.0)	
3	121 (30.3)	78 (28.2)	43 (35.0)	
Preoperative pain				0.001
No	287 (71.8)	212 (76.5)	75 (61.0)	
Yes	113 (28.3)	65 (23.5)	48 (39.0)	
Premedication				0.907
No	362 (90.5)	251 (90.6)	111 (90.2)	
Yes	38 (9.5)	26 (9.4)	12 (9.8)	
Type of surgery				0.807
UKA	81 (20.3)	57 (20.6)	24 (19.5)	
TKA	319 (79.8)	220 (79.4)	99 (80.5)	
Type of anesthesia				0.007
SAMO-PI-NB	71 (17.8)	60 (21.7)	11 (8.9)	
SA-PI-NB	299 (74.8)	199 (71.8)	100 (81.3)	
GA-PI/NB	30 (7.5)	18 (6.5)	12 (9.8)	
Operative time (min)	79.7 ± 31.3	78.5 ± 30.8	82.5 ± 32.2	0.241
Tourniquet time (min)	75.9 ± 25.9	75.1 ± 25.5	77.7 ± 26.7	0.363
Postoperative analgesics				0.025
Analgesics = 4 drugs[#]	275 (68.8)	200 (72.2)	75 (61.0)	
Analgesics < 4 drugs	125 (31.3)	77 (27.8)	48 (39.0)	

[#]Analgesics 4 drugs included opioids, acetaminophen, nonsteroidal anti-inflammatory drugs, and gabapentinoids

Data are presented as mean±SD or number and percentage (%). NRS=numeric rating scale score; ASA=American Society of Anesthesiologists; UKA=unicompartmental knee arthroplasty; TKA=total knee arthroplasty; SAMO-PI-NB=spinal anesthesia (SA) plus intrathecal morphine, periarticular infiltration (PI) and peripheral nerve block (NB); SA-PI-NB=SA plus PI and NB; GA-PI/NB=general anesthesia plus PI with or without NB

The incidence of moderate-to-severe pain after KA is shown in Figure 1. Approximately half of patients experienced moderate-to-severe pain on the first postoperative day, and about 20% of patients still had moderate-to-severe pain on the third postoperative day. Eight of the 400 patients reported moderate-to-severe pain at all postoperative day 1, 2 and 3. Thirty-seven (9.3%) patients were completely pain free (NRS=0) within the first 72 hours after surgery.

When comparing the moderate-to-severe pain group and the no or mild pain group, only preoperative pain, type of anesthesia, and postoperative analgesic drugs were significantly different between the two groups in univariable analysis. Patients with moderate-to-severe pain more frequently received GA plus PI with or without NB and SA plus PI and NB, whereas those with no or mild pain more frequently received SA plus MO, PI and NB. Those with moderate-to-severe pain were also more likely to have had preoperative pain. With regard to postoperative analgesic drugs, those with moderate-to-severe pain more frequently received postoperative analgesics < 4 drugs. The factors from univariable analysis with a *p*-value less than 0.2, including preoperative pain (p=0.001), type of

anesthesia (p=0.007), and postoperative analgesic drugs (p=0.025), were included in multivariable analysis (Table 2). Despite its p-value of 0.807, type of surgery was still included in multivariable analysis because we considered it a factor of interest. The results revealed preoperative pain (AOR, 2.10; 95% CI, 1.31-3.35; p=0.002) and type of anesthesia (AOR, 2.79 for Group SA-PI-NB; 95% CI, 1.39-5.60; p=0.004, and AOR, 3.42 for Group GA-PI/NB; 95% CI, 1.27-9.20; p=0.015; when using Group SAMO-PI-NB as a reference) to be independent risk factors for moderate-to-severe pain during the first postoperative day.

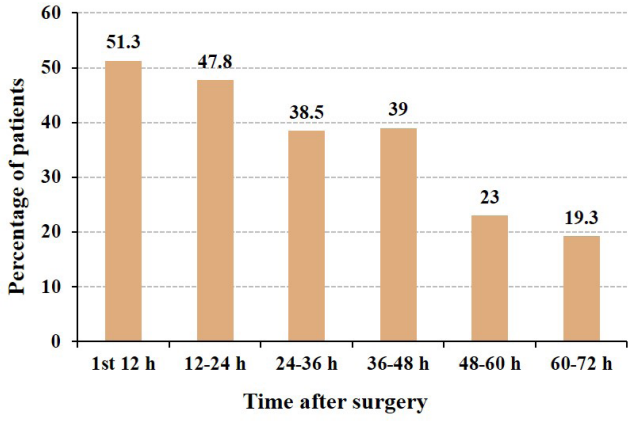


Fig 1 Incidence of moderate-to-severe pain at each postoperative time interval. Pain intensity was measured by a numeric rating scale (NRS) using maximum NRS; mild (NRS = 1-3), moderate (NRS = 4-6), and severe (NRS = 7-10) pain

Table 2 Risk factors for moderate-to-severe pain after knee arthroplasty

	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Preoperative pain	2.09 (1.32-3.30)	0.001	2.10 (1.31-3.35)	0.002
Type of surgery				
UKA	1		1	
TKA	1.07 (0.63-1.82)	0.807	0.94 (0.54-1.62)	0.814
Type of anesthesia				
SAMO-PI-NB	1		1	
SA-PI-NB	2.74 (1.38-5.44)	0.004	2.79 (1.39-5.60)	0.004
GA-PI/NB	3.64 (1.37-9.62)	0.009	3.42 (1.27-9.20)	0.015
Postoperative analgesics				
Analgesics = 4 drugs[#]	1		1	
Analgesics < 4 drugs	1.66 (1.06-2.60)	0.025	1.54 (0.97-2.45)	0.068

[#]Analgesics 4 drugs included opioids, acetaminophen, nonsteroidal anti-inflammatory drugs, and gabapentinoids

OR=odds ratio; CI=confidence interval; UKA=unicompartmental knee arthroplasty; TKA=total knee arthroplasty; SAMO-PI-NB=spinal anesthesia (SA) plus intrathecal morphine, periarticular infiltration (PI) and peripheral nerve block (NB); SA-PI-NB=SA plus PI and NB; GA-PI/NB=general anesthesia plus PI with or without NB

In Table 3, patients in Group SAMO-PI-NB had a higher incidence of pruritus than patients in Group SA-PI-NB and Group GA-PI/NB (p<0.001). No differences in nausea, vomiting, or dizziness were found among the three anesthetic groups. No evidence of respiratory depression was observed in this study.

Table 3 Adverse effects

	Group SAMO-PI-NB (n = 71)	Group SA-PI-NB (n = 299)	Group GA-PI/NB (n = 30)	*p*-value
Nausea				0.767
No	58 (81.7)	254 (84.9)	26 (86.7)	
Yes	13 (18.3)	45 (15.1)	4 (13.3)	
Vomiting				0.742
No	58 (81.7)	255 (85.3)	26 (86.7)	
Yes	13 (18.3)	44 (14.7)	4 (13.3)	
Pruritus				< 0.001
No	63 (88.7)	297 (99.3)	29 (96.7)	
Yes	8 (11.3)	2 (0.7)	1 (3.3)	
Dizziness				0.377
No	69 (97.2)	296 (99.0)	30 (100.0)	
Yes	2 (2.8)	3 (1.0)	0 (0.0)	

Data are presented as number of patients and percentage (%). SAMO-PI-NB=spinal anesthesia (SA) plus intrathecal morphine, periarticular infiltration (PI) and peripheral nerve block (NB); SA-PI-NB=SA plus PI and NB; GA-PI/NB=general anesthesia plus PI with or without NB

Discussion

Based on data derived from routine clinical practice, this retrospective chart review found a high incidence of moderate to severe pain after knee arthroplasty. A majority of patients (about 50%) experienced moderate-to-severe pain on the first postoperative day. The independent risk factors associated with moderate-to-severe pain were preoperative pain and type of anesthesia.

Almost 30 years ago, a published pain management study revealed that 60% of patients reported severe pain, and 30% reported moderate pain after TKA.[19] Similarly, two studies in pain after KA[12, 17] reported that 58% of TKA patients suffered moderate-to-severe pain on the first postoperative day, which declined to 43% by the third day after surgery. In another study that set forth to identify predictors of postoperative pain, 26% and 43% of TKA patients had moderate-to-severe pain at rest and with activity, respectively.[15] In the present study, about 50% of patients experienced moderate-to-severe pain on the first postoperative day, which is comparable to previous reports.[12, 17, 19] This finding indicates that a considerable number of patients remained suffering from moderate-to-severe postoperative pain, and postoperative pain control in routine clinical practice is still inadequate for all patients. Moreover, the results of this study highlight the need for improvement in postoperative pain management after KA. Importantly, in order to improve the quality of pain management, the individual factors associated with pain severity should be identified.

In the present study, preoperative pain was found to be a significant risk factor for moderate-to-severe pain after KA. Patients who had preoperative pain were 2.10 times more likely to have moderate-to-severe pain than were those who had no preoperative pain. Similarly, previous studies reported preoperative pain to be an important risk factor for postoperative pain intensity. In 2003, Brander et al[20] identified heightened preoperative pain as an independent risk factor for pain after TKA. In 2012, Liu et al[15] identified increased severity of preoperative pain at the surgical site as a predictor for increased risk of moderate-to-severe pain at rest and during activity. Likewise, Rakel et al[21] found high preoperative pain to be a significant predictor of moderate or severe movement and resting pain after TKA. In 2016, Thomazeau et al[22] reported that preoperative resting pain intensity was associated with the intensity of postoperative resting pain after TKA and UKA. A recent meta-analysis[23] found preoperative pain

to be a significant predictor for poor postoperative pain control. As mentioned above, preoperative pain has long been recognized as a significant risk factor for postoperative pain. Given the plethora of evidence that supports the relationship between preoperative and postoperative pain, this group of patients should be identified and the appropriate pain control should be applied before surgery.

On the first postoperative day, the present study identified type of anesthesia as a strongest risk factor for moderate-to-severe pain after KA. Patients in Group GA-PI/NB were 3.42 times more likely to have moderate-to-severe pain than those in Group SAMO-PI-NB. This finding reflects that SA plus MO, PI and NB is superior to GA plus PI with or without NB. Similarly, a systematic review[24] found that regional anesthesia for TKA decreased postoperative pain and morphine consumption when compared with general anesthesia. One retrospective study[25] that compared different types of anesthesia (GA, GA plus FNB, SA, SA plus FNB, SA plus MO, and SA plus MO and FNB) found that GA was associated with higher morphine consumption, whereas the combination of SA with MO and FNB was associated with less morphine consumption. In contrast to the present study, a cohort study[26] that compared general, regional, and combination anesthesia in knee arthroplasty found that the combination of general and peripheral anesthesia was associated with lower postoperative pain scores and less opioid consumption on the first postoperative day. However, the disparity among reported results heightens the challenge of managing acute pain after KA. GA plus PI and NB may be a useful alternative method for patients who have contraindications to neuraxial anesthesia.

When comparing SAMO-PI-NB with SA-PI-NB, patients in SA-PI-NB group were 2.79 times more likely to have moderate-to-severe postoperative pain than those in SAMO-PI-NB group. This finding is consistent with a recently published study. A prospective RCT study that compared three anesthetic techniques for TKA[27] showed that patients receiving local infiltration analgesia (LIA) plus active ACB plus MO had the best postoperative analgesia compared with those receiving LIA plus placebo ACB and LIA plus active ACB. In contrast, two other studies comparing LIA with intrathecal morphine during TKA[28, 29] found that LIA provided better postoperative pain control than intrathecal morphine. In a meta-analysis of 185 patients,[30] the results showed that FNB provided equal postoperative analgesia compared with intrathecal morphine after TKA. As stated earlier, such controversy regarding intrathecal morphine still persists. Although the present study found spinal anesthesia plus MO, PI and NB to be superior to spinal anesthesia plus PI and NB, and general anesthesia plus PI with or without NB, it is more commonly associated with opioid-related adverse effects. In the present study, the incidence of pruritus was significantly higher in Group SAMO-PI-NB than in Group SA-PI-NB and Group GA-PI/NB. No significant difference was found regarding the occurrence of nausea, vomiting, or dizziness. Also, there was no respiratory depression observed in this study. However, there is growing concern about opioid-related adverse effects, which may result in delayed ambulation and rehabilitation. The current trend in UKA and TKA pain management is moving toward multimodal analgesia with the aim of reducing opioid use.

Multimodal analgesia is gaining increased attention as an effective pain management for KA. It involves the combination of different anesthetic and analgesic techniques, such as neuraxial anesthesia, NB, PI, and multimodal oral and intravenous analgesics.[31, 32] In general, oral and intravenous analgesic drugs can be acetaminophen, opioids (short- and long-acting), NSAIDs, and gabapentinoids. Postoperative analgesics include different classes of analgesics to produce additive or synergistic effects while reducing adverse effects from individual analgesics, especially opioids.[33] In the present study, there is a variety of postoperative analgesics that are used in routine clinical practice. Some patients received only one analgesic, whereas the others received more than 1 class of analgesic drugs. Specifically, 68.8% of patients received four different drugs postoperatively, whereas 31.2% of them

received less than four drugs. Although postoperative analgesics were not identified as an independent risk factor for moderate-to-severe pain in multivariable analysis, the significant association with moderate-to-severe pain identified in univariable analysis may warrant the important role of the combined use of different analgesics as a part of a multimodal analgesia. Further investigation to explore the impact of different analgesic drugs on postoperative pain after KA is needed.

Taken together, the results of this study provide additional real-life evidence relating to the management of acute postoperative pain after KA. The high incidence rate of moderate-to-severe pain indicates the need for further improvement in pain control in this patient population. Our identification of preoperative pain and type of anesthesia as the predictors that foretell postoperative moderate-to-severe pain suggests that these factors should be central to any pain management strategy.

The present study has some limitations. First, the retrospective nature of the study may provide inadequate data for analysis, so real-life prospective study may be required. Second, the small number of subjects in some groups may have induced some bias. Given these acknowledgements, the results of the study should be interpreted with caution. Finally, due to a lack of data, this study cannot report the impact of anesthetic and analgesic techniques on rehabilitation and functional outcomes after KA.

Conclusions

This retrospective study identified a high incidence of moderate-to-severe pain after KA. Most patients experienced moderate-to-severe pain on the first postoperative day. Preoperative pain and type of anesthesia were independent risk factors for moderate-to-severe pain after KA. Future prospective study in daily clinical practice should be conducted to identify more effective pain management for KA.

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